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Office of Agricultural Biotechnology

Minutes

Agricultural Biotechnology Research Advisory Committee

March 11-13, 1992

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U.S. DEPARTMENT OF AGRICULTURE
Agricultural Biotechnology Research Advisory Committee
Minutes of Meeting
March 11-13, 1992

Time, Place, and Participants

A meeting of the Agricultural Biotechnology Research Advisory Committee (ABRAC) took place March 11, 12, and 13, 1992, in the Georgetown Room of the Rosslyn Westpark Hotel at 1900 North Fort Myer Drive in Arlington, VA. The meeting had been announced in the Federal Register and was open to the public.

Members present included:

A. David Kline, State University of New York, New Paltz, NY;

William Witt, Food and Drug Administration, National Center for Toxicological Research, Jefferson, AR;

Anne Vidaver, University of Nebraska, Lincoln, NE;

Deborah Letourneau, University of California, Santa Cruz, CA;

David Andow, University of Minnesota, St. Paul, MN;

Stanley Pierce, Rivkin, Radler & Kremer, Uniondale, NY;

Walter A. Hill, Tuskegee University, Tuskegee, AL;

Ronald R. Sederoff, North Carolina State University, Raleigh, NC;

Anne R. Kapuscinski, University of Minnesota, St. Paul, MN;

Susan Harlander, University of Minnesota, St. Paul, MN;

Edward P. Bruggeman, National Audubon Society, Washington, DC;

Alvin Young, Executive Secretary and Director, Office of Agricultural Biotechnology, U.S. Department of Agriculture, Washington, DC.

U.S. Department of Agriculture (USDA) Office of Agricultural Biotechnology (OAB) staff present included Maryln Cordle, Martha Steinbock, Marti Asner, Barry Stone, Eva Russnak, and Daniel Jones (March 13 only). Others present are listed in Appendix A.

March 11, 1992

Call to Order and Preliminaries

Dr. Young called the meeting to order at 9:15 a.m. He noted that the new ABRAC chair had not yet been announced, briefly reviewed the history of the ABRAC, and welcomed Acting Assistant Secretary of Agriculture for Science and Education Dr. Harry Mussman.

Dr. Mussman said that he had met with Dr. Young and former ABRAC chair Dr. Bennie Osburn the previous day, and that Dr. Osburn had presented him with the long-awaited ABRAC recommendations for the Proposed Guidelines for Research Involving Planned Introduction into the Environment of Genetically Modified Organisms (hereafter referred to as the Guidelines).

Dr. Mussman outlined some of the future issues ABRAC may address, including:

- transgenic fish projects;
- Animal and Plant Health Inspection Service (APHIS) biotechnology programs;
- Food Safety and Inspection Service (FSIS) efforts to deal with the slaughter of transgenic animals; and
- the biotechnology risk assessment research program mandated by the 1990 Food, Agriculture, Conservation and Trade Act (hereafter referred to as the 1990 Farm Bill).

Dr. Mussman also noted that ABRAC's counsel may be needed as USDA attempts to set priorities under the President's Biotechnology Research Initiative.

Dr. Mussman designated A. David Kline as the new chair of the ABRAC, and Anne K. Vidaver as vice chair.

Dr. Mussman and Dr. Kline presented certificates of appointment to the following ABRAC members:

William Witt, veterinary/animal science;

Anne K. Vidaver, plant science;

Ronald Sederoff, forestry;

Anne R. Kapuscinski, animal science;

Walter Hill, plant science;

Susan Harlander, microbial science and food science;

Stanley Pierce, law and regulation; and

Edward Bruggeman, ecology and environmental policy.

Dr. Young introduced Lisa Zannoni, who is an assistant to the Deputy Secretary of Agriculture, and a former assistant to the Assistant Secretary for Science and Education. He also introduced OAB staffers Martha Steinbock, Marti Asner, and Barry Stone.

Dr. Young explained how OAB prepares the agenda for each ABRAC meeting, and outlined the agenda for the next three days. The ABRAC approved the agenda.

Dr. Kline turned the discussion to the minutes of the December, 1991, meetings of the Classification and Confinement Working Group and the full ABRAC. Dr. Young noted that former ABRAC Chair Osburn had recommended that those minutes be approved.

Dr. Vidaver moved that the minutes for the meeting of the Classification and Confinement Working Group be approved without change. Dr. Hill seconded the motion, which passed unanimously.

Dr. Young explained that the minutes for the December meeting of the full ABRAC included a supplement consisting of the ABRAC's recommended Guidelines. He said that when approved, both the minutes and the supplement would be distributed. The next step would be for the U.S. Department of Agriculture (USDA) to publish the recommended Guidelines in the Federal Register.

Dr. Vidaver asked that the term "environmental impact" be used in the middle paragraph of page 7 of the minutes. Dr. Kapuscinski suggested that the word "defeated" be substituted for the term "voted down" on page 13.

Dr. Witt moved that the minutes for the December meeting of the full ABRAC be accepted with the suggested changes. Dr. Hill seconded the motion, which was approved unanimously.

Dr. Kapuscinski asked whether the Guidelines would be distributed before USDA's Office of the Secretary decided whether to implement them. Dr. Young responded that the Federal Advisory Committee Act requires the ABRAC to publish and distribute minutes of its meetings to the public. The Guidelines will be distributed as ABRAC's recommendations. Dr. Young also said that he expected the Guidelines to be published by USDA in the Federal Register.

Dr. Kline asked Dr. Young to review the ABRAC charter and ABRAC procedures.

Review of ABRAC Charter and Procedures

Dr. Young said that the new ABRAC charter had been signed by Secretary of Agriculture Edward Madigan on January 16, 1992. He noted that while ABRAC reports to the Office of the Secretary through the Assistant Secretary for Science and Education, other Assistant Secretaries also may interact with the ABRAC.

In reviewing how the ABRAC is organized, Dr. Young noted that although the ABRAC charter allows five members to be Federal employees, Secretary Madigan had decided that only one member should be a Federal employee. The ABRAC, he said, meets four times per year, and has an annual budget of $145,000.

Dr. Kapuscinski asked when ABRAC meetings might be closed to the public. Dr. Young replied that closed meetings would be convened if confidential business information were to be discussed. The closure would have to be announced in the Federal Register. He noted that the ABRAC has never held a closed meeting.

With regard to ABRAC procedures, Dr. Young explained that the procedures had been written when the ABRAC consisted of 12 members and 12 alternate members; however, ABRAC no longer has alternates. Therefore, Dr. Young suggested that the procedures be amended to remove any references to the alternates.

Other suggested changes to the procedures included the following:

- Adding proposed dates for the next three ABRAC meetings: June 10-12, 1992; September 23-24, 1992; and December 9-11, 1992.
- Inserting the phrase "and honoraria" in item 4 after the word "reimbursement."
- Defining a quorum as the presence of at least eight ABRAC members (item 7).
- Substituting the word "vice chair" for "co-chair" (item 15).
- Adding the phrase "the ABRAC" after the reference to the National Biological Impact Assessment Committee in item 9.

Procedural items regarding conflict of interest, confidential business information, and the need for closed sessions generated some discussion among the ABRAC members. Dr. Kline asked Dr. Pierce, Dr. Hill, and Dr. Vidaver to draft procedural language with regard to conflict of interest. Dr. Young promised to try again to see if USDA would approve a statement with regard to confidential business information, and to present the statement at the next ABRAC meeting.

Dr. Kline asked Dr. Young to discuss the Presidential Biotechnology Research Initiative.

Presidential Biotechnology Research Initiative

Dr. Young presented the publication Biotechnology in the 21st Century, which outlines the Presidential Biotechnology Research Initiative.

In 1976, Congress required the President to appoint a science advisor and establish a Federal Coordinating Council for Science, Engineering, and Technology (FCCSET). The White House Office of Science and Technology Policy (OSTP) works with FCCSET committees and subcommittees. Among those subcommittees is the Biotechnology Research Subcommittee, which developed the biotechnology initiative.

The biotechnology initiative proceeds from a relatively broad definition of biotechnology developed in 1984 by the Congressional Office of Technology Assessment (OTA). The initiative uses this definition to present an inventory of biotechnology research and programs conducted by the Federal government.

Among the Federal agencies which deal with biotechnology are the Agency for International Development (AID); Department of Commerce; Department of Energy; Department of Defense; Department of the Interior; Department of Justice; Department of Health and Human Services; Department of Veterans Affairs; U.S. Environmental Protection Agency (EPA); National Aeronautics and Space Administration (NASA); National Science Foundation; and USDA.

Within USDA, 13,000 scientists in four agencies implement a $1.3 billion research operating budget. The four agencies are the Agricultural Research Service (ARS); Cooperative State Research Service (CSRS); Forest Service (FS); and Economic Research Service (ERS).

Of the $3.4 billion in Federal money spent on biotechnology research in 1991, health research accounted for 42 percent, and general/foundation research accounted for 37 percent. Infrastructure (including USDA facilities) accounted for 8 percent; agriculture, 5 percent; manufacturing and bioprocessing, 3 percent; environment, 2 percent; and energy, 2 percent.

Suggested priorities include increasing investments in interdisciplinary research, environmental research, and processing research; strengthening and establishing programs to study organisms not currently under investigation; and supporting foundation research.

Applications for agricultural biotechnology research include new, improved agricultural products; improved crops and animals; new uses for crops; better management of agricultural ecosystems; better tools for diagnosing diseases; and improved control of microbial pests.

Dr. Young outlined Federal investment in agricultural biotechnology as follows:

Table 1: Federal investment in biotechnology, $ million

AGENCY	FY '91	FY '92	FY '93
USDA	106.4	114.5	119.5
NSF	25.6	28.7	35.0
HHS	25.6	28.9	30.8
AID	7.6	9.4	12.7
NASA	4.3	4.2	4.4
Commerce	3.0	3.0	3.0
DOE	1.7	1.8	2.1
TOTAL	174.2	190.5	207.5

Among USDA investments in biotechnology research, plants receive the lion's share of funding, followed by animals, aquaculture, and food science (including food safety).

Dr. Young said that with the completion of the inventory on Federal biotechnology, the next task is how to prioritize that research. The ABRAC has a vital role to play in helping USDA make its recommendations. Current USDA priorities include gene mapping, pest management, animal health and welfare, crops and biomass, new processing technology, food safety, and waste management and use.

Dr. Young presented some examples of the issues being faced in biotechnology research:

- USDA is investing almost nothing in general/foundation research, although the National Research Initiative is attempting to correct this.

- USDA is doing virtually no biotechnology research related to nutrition.

- While health research receives billions of dollars in funding, environmental research receives only a few million dollars.

After a break for lunch, Dr. Kline invited Dr. Edward Wilson to discuss the CSRS Biotechnology Risk Assessment Program.

CSRS Biotechnology Risk Assessment Program

Dr. Wilson said that CSRS is funding at least four risk assessment pilot projects: a canola seed survival project in Montana; a canola pollen dispersal project in Wisconsin; a cotton pollen dispersal project; and a Rhizobium/soybean project.

Dr. Wilson directed the ABRAC's attention to Section 1668 of the 1990 Farm Bill, which requires the Secretary of Agriculture to develop a biotechnology risk assessment program. Funding for the program was set at 1 percent of agricultural biotechnology research funding.

Implementing this program, Dr. Wilson said, required addressing two challenges:

1. How should biotechnology be defined for the purposes of this program? Although some favored a narrow definition, Secretary Madigan decided in February 1992 to use the relatively broad definition developed by OTA in 1984.

   According to Biotechnology in the 21st Century, USDA is spending $140.5 million for biotechnology research. Therefore, $1.4 million should be spent for risk assessment.

2. Where will the $1.4 million come from? Based on the spending totals outlined in Biotechnology in the 21st Century, ARS must contribute $773,000; CSRS must contribute $589,000; and FS must contribute $43,000.

Dr. Wilson said that a coordinating committee consisting of representatives from APHIS, EPA, OAB, CSRS, ARS, and FS recommended research areas to be covered in the first year of the risk assessment research grants program. He asked that the ABRAC submit recommendations of its own — but noted that CSRS wants to complete the funding process by September 30, 1992.

Dr. Kline suggested that the ABRAC use the coordinating committee recommendations as a starting point for its own discussion.

Drs. Vidaver and Kapuscinski asked if EPA performs risk assessment research. Dr. Blowers responded that EPA has an extensive risk assessment research plan under development in its Office of Research and Development, and that USDA works closely with that office. Dr. Young added that EPA's emphasis is microbial, as required under the Toxic Substances Control Act (TSCA) and the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).

Dr. Sederoff expressed concern with the coordinating committee's recommendations. He felt that some of the recommendations were much too specific, and said that they only dealt with short-term crises. He said that a more fundamental approach would be appropriate.

Ms. Steinbock pointed out that the legislation which creates the program focuses on very practical concerns. Moreover, the European Community has many basic risk assessment research programs in place – but European regulators are not finding the research very useful.

Dr. Young agreed, and pointed out that the presence of several regulatory agencies on the coordinating committee might have influenced the recommendations. Those agencies need information on the research questions proposed.

Dr. Bruggeman pointed out that specificity is needed because the program has relatively little funding at $1.4 million.

Dr. Sederoff asked what the professional level of the peer review panelists would be. Dr. Wilson responded that those details had not been worked out. Dr. Sederoff pointed out that the composition of the peer review panels was an important issue. Dr. Wilson agreed and said that the NRI peer review panels would be a model for the risk assessment panels.

Dr. Kapuscinski expressed concern with applying the broad term "genetically modified organism" (as featured in the OTA definition of biotechnology) to fish. She said that such broadness could result in the receipt of many proposals which would have little to do with biotechnology risk assessment. She suggested that the request for proposals (RFP) be made more precise. Dr. Vidaver noted that page 3 of Biotechnology in the 21st Century contains examples of "new biotechnology" which could be used to make the RFP more precise.

Dr. Kapuscinski also recommended an addition to the coordinating committee's list: development of techniques and tools for ecological risk assessment, especially to integrate different experimental approaches. Dr. Blowers said that EPA already does that.

Dr. Bruggeman pointed out that several different review panels would be needed to award these grants, and asked whether administrative costs would be prohibitive. Dr. Wilson said that no administrative costs would be deducted from the $1.4 million.

After further discussion, the ABRAC agreed that it was not in a good position to set risk assessment research priorities at the present time. Dr. Young said that the OAB staff would incorporate the ABRAC's concerns into a draft letter to Dr.

Wilson, and would submit the letter to the ABRAC at the Friday session.

Drs. Kline and Young then invited Dr. Ann Lichens-Park to discuss other CSRS biotechnology activities.

CSRS Biotechnology Activities

Dr. Lichens-Park began by discussing the National Biological Impact Assessment Program (NBIAP), which is designed to facilitate and assess the safe application of new techniques for genetically modifying plants, animals, and microorganisms to benefit agriculture and the environment. NBIAP projects provide information resources and enabling resources to scientists, and general information to the public.

Among NBIAP's resources are an electronic bulletin board, a newsletter with over 7,000 subscribers, and a database.

Other CSRS biotechnology activities include the cosponsoring of conferences, the award of research grants and the coordination of regional projects.

Dr. Young thanked Dr. Lichens-Park, and asked Dr. Arthur Kelman to discuss the National Research Initiative (NRI).

National Research Initiative

Dr. Kelman told the ABRAC that its decisions will affect whether biotechnology's promise is realized, which in turn will affect many of the decisions to award competitive grants under the NRI. He also noted that the NRI is small compared to most research plans, including USDA's research initiatives, but there is hope that it will grow.

The NRI, Dr. Kelman said, was initiated thanks to a unique consensus among commodity groups and scientific societies, which prompted Congress and the Office of Management and Budget (OMB) to agree to try to fund the NRI at an eventual level of $500 million. During the NRI's first year, 2,713 research proposals totaling $638.8 million were submitted. Funding was available for 590 grants totaling $69.2 million.

Dr. Kelman noted that the NRI review system is modeled after the review systems of the National Institutes of Health (NIH) and National Science Foundation (NSF). Each NRI grant application was reviewed by at least four reviewers. Close to 300 panelists have participated in the reviews. Dr. Kelman pointed out that proposals were not rejected because of poor quality, but because of funding limitations.

Dr. Kelman outlined the NRI funding allocations as follows:

Table 2: NRI Funding Allocations, Program Area, $ million

PROGRAM AREA	FY '91	FY '92
Natural Resources/Environment	14.0	18.0
Nutrition/Food Safety/Health	4.0	6.5
Plant Systems	35.0	40.0
Animal Systems	20.0	25.0
Markets, Trade, and Policy	0.0	4.0
New and Value-Added Processing	0.0	4.0
TOTAL	73.0	97.5

Dr. Kapuscinski asked Dr. Kelman for an example of biocontrol research. Dr. Kelman responded that many organisms in greenhouses and laboratories inhibit other organisms.

Dr. Young invited Dr. Jerome Miksche of ARS to discuss his agency's biotechnology activities.

ARS Biotechnology Activities

Dr. Miksche said that ARS has 2,500 scientists at 122 locations who operate a research budget of over $620 million. The agency sets research priorities by considering current Administration and agency policies; directives of Congress and other interests; and national agricultural problems and issues. ARS also is aware of emerging agricultural problems and needs, and considers recommendations from external groups in the agricultural community, action agencies within USDA, scientists, and ARS line managers. The agency also factors in analyses of current ARS and other USDA programs and capabilities.

Dr. Miksche said that ARS believes a positive public perception of biotechnology is crucial to bringing research results to the public. Although biotechnology's biggest contribution is expected to be in research on crops, livestock, and post-harvest technology, biotechnology also contributes to research on human nutrition and resource conservation.

Dr. Miksche noted that biotechnology can help to:

- Reduce and eliminate the effects of natural and artificial pollutants in soil and water;
- Enable plants to adapt to marginal growing conditions;

- Develop higher-quality, more stress-resistant crops;
- Develop higher-quality, more stress-resistant livestock;
- Develop more effective tests for diagnosing animal diseases;
- Produce better ways to prevent animal diseases;
- Improve reproductive technology;
- Improve food safety and quality;
- Enhance non-food uses of crops, and develop new uses for agricultural products; and
- Determine exactly what nutrients the human body needs, particularly with respect to at-risk populations.

Dr. Miksche also discussed the ARS plant genome program, the coding of ARS biotechnology projects, and projects involving recombinant DNA. He noted that the FY '92 ARS biotechnology research budget totals $69.5 million, of which $25.4 million is allocated to plants, $23.8 million to animals, $3.8 million to insects, and $16.5 million to microorganisms.

Dr. Young thanked Dr. Miksche for his presentation and invited Dr. Stanley Krugman to discuss Forest Service (FS) biotechnology activities.

FS Biotechnology Activities

Dr. Krugman said that FS biotechnology activities began in the mid-1970's with a grants program designed to determine if new technology could be applied to woody plants. By 1980, the first significant grants were issued.

More recently, FS recombinant DNA research funding totaled $4 million in FY '91 and $5 million in FY '92. Requested funding for FY '93 totals $8.5 million.

FS biotechnology research, said Dr. Krugman, is looking at several areas. One area deals with putting viruses to beneficial uses such as controlling gypsy moth infestations. Another addresses alleviating wilt diseases in trees. A third area deals with accelerating the life cycle of the tree so that forest improvement does not take as long as is the case with traditional methods. The fourth area focuses on genome mapping in some major tree species, where considerable progress has been made. Other programs deal with disease and stress to trees, and development of advanced tissue culture techniques.

Dr. Kline invited Dr. John Reilly of the Economic Research Service (ERS) to discuss his agency's biotechnology activities.

ERS Biotechnology Activities

Dr. Reilly said that ERS spends about $200,000 on biotechnology activities per year. The agency's biotechnology activities concentrate on technological assessment, policy and technology issues, and forces that affect the rate of technological change.

ERS's biotechnology activities started during the period when bovine somatotropin (BST) became controversial. Dr. Reilly expressed the view that BST and other growth hormones were oversold early in their development, and that this overselling created unrealistic fears of the socioeconomic effects of such technology. According to Dr. Reilly, the technology actually has not had any serious economic effects. With specific regard to milk, the Nation's milk marketing order program would moderate the effects of any BST-induced growth. In addition, biotechnology fits within the Nation's regulatory system.

Dr. Reilly concluded by saying that ERS is working with ARS and the Agricultural Research Institute (ARI) to survey private sector spending on research and development (R&D), including agriculture.

Dr. Kline asked what ERS could do to bring its research results to the attention of the public. Dr. Reilly responded that the agency doesn't have a formal education program (except for its Agricultural Information Bulletin), but relies on the Extension Service to deliver research information to the public. Dr. Young noted USDA's Biotechnology Council is trying to develop a public information plan.

Dr. Kline thanked Dr. Reilly for his presentation and invited Dr. Marvin Norcross to discuss the biotechnology activities of the Food Safety and Inspection Service (FSIS).

FSIS Biotechnology Activities

Dr. Norcross said that FSIS had developed a Federal Register notice and document regarding decision criteria for evaluating nontransgenic animals that result from transgenic animal research, and thanked the ABRAC for its help in developing the criteria. He said that the next step would be to develop decision criteria for transgenic animals resulting from such research, and asked for the ABRAC's counsel during that process.

Dr. Norcross explained that FSIS has a $450 million budget, with 7,400 inspectors at 6,500 plants. Its mission is to ensure the

safety and wholesomeness of the Nation's meat and poultry products. The agency tries to be pro-active and anticipate future food safety and quality issues and problems.

Dr. Vidaver asked about the status of seafood inspection. Dr. Norcross said that several bills requiring inspection of seafood failed to pass Congress. The Food and Drug Administration (FDA) and the Department of Commerce operate a voluntary fish inspection program that is working well.

Dr. Norcross said that the document on transgenic animals being developed by FSIS will address fish.

Dr. Young asked how FSIS's policy with regard to animals would be affected if FDA puts a transgenic food policy in place. Dr. Norcross explained that EPA currently sets standards for pesticide tolerances, and that FDA sets standards for drug tolerances. FSIS uses those tolerances to determine whether the products it inspects are safe to eat. That scheme should work for both transgenic and non-transgenic animals, he said.

Ms. Steinbock asked for topic ideas for an upcoming international biosafety conference in The Netherlands. Dr. Norcross suggested a session on additives to animal products, and Dr. Berkowitz suggested a discussion of the principles of animal adaptation.

Dr. Kline invited Ms. Steinbock to update the ABRAC on international activities.

International Activities

Ms. Steinbock said that USDA's international biotechnology activities have three goals: achieve biosafety, establish a level playing field in the international marketplace, and seek partnerships with other countries on mutually beneficial projects.

Biosafety activities include working with the Organization for Economic Cooperation and Development (OECD) on projects such as setting safety norms for small-scale and large-scale field tests, and developing food safety principles countries could use to determine the safety of foods that move through international trade channels.

With regard to trade, the big issue is BST. The Office of the U.S. Trade Representative (USTR) is working with the Commission of the European Community (EC) to resolve the so-called "fourth criteria" controversy. Although the Commission has officially backed away from the idea of restricting imports of products with BST for social or economic reasons, an EC moratorium on marketing BST products recently was extended for two more years.

Examples of scientific cooperation include the U.S.-EC Task Force on Biotechnology Research, which focuses on policy issues and increasing public understanding of biotechnology. An upcoming workshop in Dublin, Ireland, will focus on improving communications to the public on biotech issues.

Dr. Kline asked whether U.S. manufacturers are testing their biotechnology products outside the United States in order to dodge government regulation. Ms. Steinbock replied that reports of such activity are overstated. Ms. Cordle said the reverse is truer: Europe and Japan often try to test their products in the United States because U.S. regulations are so much less restrictive than theirs.

Dr. Kapuscinski asked what the Food and Agriculture Organization (FAO) of the United Nations is doing with respect to biotechnology. Ms. Steinbock replied that every UN agency is interested in biotechnology, and that FAO is trying to develop an international code of conduct on biotechnology. The United States does not favor a code of conduct, which would be legally binding.

Dr. Kline thanked Ms. Steinbock, and recessed the ABRAC for the day at 4:35 p.m.

March 12, 1992

Dr. Kline reconvened the meeting at 9:15 a.m., and introduced Drs. Letourneau and Andow, who had not attended the previous day's session. Dr. Young introduced Ms. Cordle and Ms. Russnak, and Dr. Kline asked the guests to introduce themselves.

Dr. Kline then asked Ms. Cordle to share with the ABRAC some background information on Auburn University's transgenic catfish proposal.

<u>Transgenic Catfish Proposal: Background</u>

Ms. Cordle noted that USDA is interested in investing in aquaculture, and that the Presidential Initiative on Biotechnology singled out marine biology as a priority area.

Auburn's transgenic catfish study is identical to its earlier transgenic carp study except that a different fish species is involved, and a larger number of fish are involved.

CSRS received the catfish proposal October 23, 1991. In that proposal, Auburn University asked for USDA approval to use Hatch Act funding for the experiment. CSRS Administrator Dr. John

Patrick Jordan met with Dr. Young and Ms. Cordle and named Ms. Cordle project leader. Her assignment was to develop and implement a plan to consider the catfish proposal.

The plan was developed in November 1991, but because time would prevent the ABRAC from considering the proposal at its December meeting, the OAB decided to ask several fisheries consultants to review the proposal. The selected consultants have backgrounds in fishery science and ecology.

Ms. Cordle introduced the consultants: Dr. Charles Brown, USDA/APHIS; Dr. Meryl Broussard, USDA/CSRS; Dr. Nick Parker, Texas Tech University; and Mr. William Reeves, Alabama Department of Conservation and Natural Resources. Two other team members — Dr. Harold Kincaid, National Fisheries and Wildlife R&D Laboratory, and Dr. Ernie Brannon, University of Idaho — were unable to attend the ABRAC meeting.

The consultants met in Washington on January 28, 1992, to discuss the Auburn proposal. Their recommendations were sent to Dr. Jordan in a letter dated February 28, 1992.

Dr. Jordan also received three letters which objected to the Auburn proposal. These letters were from the National Wildlife Federation, the National Audubon Society, and the Sportsmen Conservationists of Texas.

Ms. Cordle asked the ABRAC to prepare a formal recommendation on the proposal. She suggested that the ABRAC identify the critical science and safety issues in the proposal, and convey its views on those issues, and the scientific basis for each of those views. She said that Dr. Jordan will consider the advice of the ABRAC, the consultants, USDA's Office of General Counsel (OGC), the objections from the three outside organizations, and the obligation of CSRS to comply with National Environmental Policy Act (NEPA) regulations in deciding whether to release Hatch Act funds for the experiment.

Ms. Cordle said that no Federal regulatory agency has chosen to exercise jurisdiction on this proposal. CSRS is evaluating the proposal to ensure that its obligations under NEPA are fulfilled before authorizing the use of Hatch Act funds.

Dr. Kline then asked Dr. Rex Dunham, principal investigator for the catfish experiment, to summarize the experiment for the ABRAC.

Summary of Transgenic Catfish Experiment

Dr. Dunham summarized the procedures for the transgenic catfish experiment, which involves spawning brood fish containing a

rainbow trout growth hormone (rtGH) gene in the hatchery and rearing offspring in outdoor ponds. As part of this summary, he also discussed Auburn's earlier experiment with transgenic carp.

There are two alternative environments in which the experiment on the catfish offspring could be conducted: 1) rearing 100,000 offspring/fry in new outdoor research ponds and reducing the number to 3,000 at the fingerling stage; or 2) rearing 10,000 catfish offspring/fry in indoor tanks and reducing the number to 3,000 at the fingerling stage before placing them in the new outdoor research ponds for continued study.

Dr. Dunham then detailed the confinement procedures that would be in effect if the catfish offspring fry were raised outdoors (Alternative 1).

The entire outdoor pond area is surrounded by an 8-foot chain link fence embedded in a concrete footer with bird netting across the top. The ponds are constructed from compacted clay with a 5-foot concrete wall around the perimeter of each pond to stabilize the banks. In addition, an 18-inch high window screen mesh attached to the fence will further prevent escape of the fish, and prevents predators from reaching them. Additional security measures include sealants to gates, barbed wire atop the fences, and signs warning that trespassers are subject to a $500.00 fine.

No predators or tracks have been seen within the facility, but raccoon tracks have been seen outside the facility.

On the cross levees is a small spillway that allows water to flow into an adjoining pond if a pond's drain becomes plugged.

Perhaps the most important security feature is the fact that the water in the ponds is static. The water level is kept 5 inches below the top of the standpipe in each pond. The overall water level in a pond is lowered whenever it exceeds that level.

Dr. Dunham recommended that the water be allowed to rise and drain naturally instead of deliberately lowering it. When the water level is deliberately lowered, head pressure increases and the screen is challenged.

Water is filtered through a set of barriers at four different locations within the pond facility: a screen on the drain pipe of each pond, at the small filter box on the common draw line for the ponds, at the large filter box in the seepage pond, and the French drain. No catfish or carp have been observed in the filter boxes of the seepage ponds.

In addition, the facility is built to withstand the effects of very large rainstorms. For example, a storm which dumped 6 inches of rain on the area filled only 10 to 15 percent of the

drainage system's capacity. In addition, the ponds are located 37 feet above the 100-year level for the Sougahatchee Creek, and an agricultural meteorologist is on staff to provide timely information on weather developments.

The drainage ditch leads to a 17-acre barrier pond stocked with bass and blue gill, both of which prey on small fish such as the catfish.

Local police and Auburn University's own security officers patrol the facility. The screens and facilities are inspected daily and weekly, and logs are maintained. In addition, the local Institutional Biosafety Committee (IBC) has made one unannounced inspection, and the local APHIS office has made several unannounced inspections. Personnel are trained and given examinations so that they are familiar with termination procedures and maintenance.

Dr. Dunham discussed data from the mirror carp and channel catfish containing the rtGH gene.

In carp, integrating the rtGH gene has varied from 1 to 10 copies at both single and multiple sites. In some individuals, deletions to the sequence occurred. Rainbow trout growth hormone was found in red blood cells as well as in other tissues of F1 transgenic carp where normally it would not be expected to appear. Tissues evaluated include eye, liver, muscle, intestine, and gonads. Variable data from inheritance studies suggest mosaicism in the parents.

In 65 percent of the carp families, 10 to 60 percent showed improved growth in the transgenic individuals. However, in some families there was no response. These results, however, are not unexpected. They show that traditional breeding and biotechnology cannot be divorced from one another. Selection will be needed to identify individuals with the right copy number inserted in the right place and expressing rtGH at the right level.

Few deformities have been observed. The deformities appeared to curb the growth of transgenic carp more than the non-transgenic carp. No tumors were found in either the transgenic carp or transgenic catfish.

Preliminary catfish data indicate that growth hormone production is temperature dependent. Higher levels of rtGH are produced in warm water than in cool water. The rtGH inheritance data for catfish show even more variation than the carp data, and mosaicism appears to be more pronounced.

Dr. Dunham concluded by noting that catfish do not like to be raised indoors. Mortality rates are far higher for indoor

catfish than for outdoor catfish – and, in fact, the carp are doing far better outdoors than they did indoors. This factor is an important reason to move the catfish experiment outdoors, as specified in Alternative 1.

Employing Alternative 1 also would increase the number of experimental fish, permit an examination of the interactions of the genotype with the environment, and provide an opportunity to verify lab data in an environment that is more typical of commercial aquaculture conditions.

Dr. Dunham reiterated that Auburn's facilities are state-of-the-art, feature lots of filtering, and employ as much or more confinement than most indoor facilities.

Dr. Kapuscinski asked Dr. Dunham if the lower survival rate of the transgenic gamete or embryo could be attributed to gene rearrangement or insufficiently low detection limits – for example, if only one copy of the gene is passed to the progeny. Dr. Dunham replied that rearrangement was a possibility, but that because DNA probes were used, he thought deletion was more likely. Insufficiently low detection limits were not a factor because analysis PCR amplification was used in the analysis.

Dr. Bruggeman asked if the survival rate for the carp was calculated for a single generation; Dr. Dunham said that was the case. Dr. Bruggeman then asked if the carp data were collected from outdoor facilities. Dr. Dunham said that the brood stock were held indoors for two years; fish that weighed 1.5-2.5 kg were kept outdoors.

Dr. Andow asked if the fish were separated in terms of families. Dr. Dunham said that the fish were branded and marked, and that families were held in the same pond. Dr. Andow then asked if fecundity rates related to size; Dr. Dunham said the data were adjusted by body weight.

Dr. Andow asked if there were data on relative efficiency of food conversion. Dr. Dunham replied that he was conducting such studies. He predicted, based on other breeding programs, that some of the increased growth would be attributable to increased food consumption, and another portion would be due to increased feed conversion efficiency.

Dr. Andow asked if there were plans to compare results of outdoor and indoor rearing. Dr. Dunham said such a comparison was in progress, but that he was uncomfortable with the conclusions.

With regard to PCR amplification, Dr. Kapuscinski asked how the researchers were looking for the rtGH gene. Dr. Dunham said that blotting techniques and Southern hybridizations were being used.

Dr. Kapuscinski then asked whether electrofishing detects small catfish, and how such electrofishing could eradicate existing catfish in the barrier without also eradicating predators. Dr. Dunham acknowledged that electrofishing was not perfect but that it could eradicate 1-inch fish.

Dr. Sederoff asked to what extent the transgenic fish fall within the natural range of variation of the ecosystem into which they might be accidentally released. Dr. Dunham said they fell within the normal range. The increased growth rate of 18 to 30 percent for the transgenic fish is the same as for fish bred by traditional methods.

Dr. Sederoff then asked about taxonomic similarities between carp and catfish. Dr. Dunham explained that the two fish are quite different taxonomically; they are from two different families. The carp was chosen for the first experiment because it is a warm water fish and matures faster than the catfish does, thus easing control of reproduction.

Dr. Letourneau remarked that, given the considerable variability of the experiment results, there might be no reason to continue the experiment. She suggested that the experiment was not resulting in sufficiently large differences between genetic manipulation and traditional methods to continue. Dr. Dunham responded that there are many ways to improve a trait, and that the experiment could help determine whether both methods should be used simultaneously. He also stressed the value of learning more about gene transfer, expression, and biological effects.

Dr. Letourneau asked Dr. Dunham if he had looked at changes in the movement of the transgenic fish as well as the size. Dr. Dunham said he had not, and did not know what the effects were.

Dr. Andow cautioned against simplistic mapping of genotypes and phenotypes. He suggested that environmental analysis can differ between a fish that grows faster because it ingests more and a fish that grows faster because it converts feed more efficiently.

Dr. Vidaver asked Dr. Dunham to define the term "behavior" as used in his analysis. Dr. Dunham said behavior is anything that seems abnormal, such as spatial arrangements, harvest avoidance, aggressiveness or the lack thereof. He said that behavior is difficult to document.

Dr. Vidaver then asked what normal confinement practices would be in experiments involving non-transgenic fish. Dr Dunham said that normally ponds would have a screened drain outlet. There would be no fences or seepage ponds, and only one filter system — not four, as is the case in the current experiment. Dr. Dunham said that the extra security measures probably cost about $100,000 to install.

Dr. Sederoff asked if the use of genetic selection would result in knowledge about the basic mechanism for the improved growth rate. Dr. Dunham said that in the selection experiments about 60 to 70 percent of the improved growth was attributable to increased consumption of food, and that 30 to 40 percent was due to increased feed efficiency. He added that the selection process does not look at the mechanism, but selects on the basis of body weight.

Dr. Pierce asked how the facility currently was being used. Dr. Dunham said the facility was being used for the transgenic carp experiment, and would be used for a wider-ranging fish genetics program.

Dr. Kline then introduced Dr. Charles Brown, who presented the findings of the consultants with regard to the transgenic catfish experiment.

Report of Consultants

Dr. Brown said that the consultants had concluded that if the experiment were carried out as described, no significant impact on the quality of the human environment would result. However, in reaching that conclusion the consultants did not agree totally on every issue.

All of the consultants agreed that they would be concerned if the transgenic fish were used prematurely for commercial aquaculture. The consultants also were concerned about the safety of the brood fish in the older outdoor ponds, but noted that the local IBC had approved this under the NIH Guidelines.

The consultants felt encouraged by the preliminary data and found it useful in considering the catfish proposal. However, the section of the proposal that dealt with the range of variation between transgenic and control carp and catfish needed to present more facts and be more clearly expressed.

All of the consultants agreed that Alternative 1, rearing the offspring/fry in outdoor ponds, was preferable to holding the offspring indoors until the fingerling stage. All of the consultants agreed that the possibility of escape of the catfish was not zero but nevertheless was highly unlikely. Unless a very unlikely sequence of events were to occur, there would be no threat of disruption to the Tallapoosa River ecosystem.

The consultants were concerned that the proposal contained statements that were not based on fact but actually were opinions. The consultants felt that the proposal had a tone of advocacy which diluted its objectivity.

Dr. Kapuscinski asked what percentage of the mortality rate for the catfish in the wild is pre-hatching. Dr. Parker said he did not know, but that most of the mortality would be expected to occur at an early stage of development.

Dr. Dunham said that surveys of Yates Reservoir showed that 3 percent of the catfish population was four inches long or less. Dr. Kapuscinski asked what the survival rate was for fish in the wild when they reached the 4-inch mark. Dr. Dunham said it was fairly good, but that fish should actually be 6 to 8 inches long for stocking purposes.

Dr. Andow asked what the natural hatching rate in the area was. Mr. Reeves said that he did not know, because male catfish guard the eggs in an enclosed structure. Predation occurs after birth when the young swim to the surface in a single brood. Dr. Broussard said that hatchability in controlled conditions varies, but under optimum conditions can be close to 100 percent. Dr. Broussard added that fry survival rates do not provide sufficient information with regard to determining post-escape safety; if brood fish escape, the situation would be very different.

Dr. Bruggeman, noting the February date on the data tables, asked if the consultants had this data available to them when they were preparing their report. Ms. Cordle explained that the consultants had the data January 28, and that Dr. Dunham later refined the data before wider distribution occurred.

After a lunch break, Dr. Kline invited Mr. Reeves to speak briefly to the ABRAC.

Comments of Mr. William Reeves

Mr. Reeves said that the State of Alabama agrees with the recommendations of the consultants, and is satisfied with Auburn's safety and security efforts with regard to the proposed transgenic catfish experiment. However, the State also shares the consultants' concern with the effects on the environment of a commercial strain of transgenic catfish.

In response to a question from Dr. Andow, Mr. Reeves said that quite a few fish are listed as endangered species in Alabama; the state has the country's second-highest number of endangered fish species. However, there are no endangered species in the Songahatchee Creek drainage and Yates Reservoir.

Dr. Hill asked if anyone from the Alabama Department of Conservation participated with the Auburn University IBC in monitoring activities, and if the Department would be involved in future monitoring. Mr. Reeves replied that he was part of the team that inspected the facility, that he was very impressed with

the facility, and that he would participate in future monitoring activities.

Dr. Kline then asked the ABRAC primary reviewers to comment on the proposal.

Comments of Primary Reviewers

Dr. Witt began the comments of the primary reviewers. He evaluated the proposal according to the Guidelines. He said that the level of safety concern (LSC) for the parental organism (i.e., the Tifton Channel catfish) was low, or LSC-1. The genetic modification's effect on safety was a Type 3, because the effects of the modification are not sufficiently understood to determine the level of safety. The LSC for the modified organism is 2, because although the modification increases concern to the extent that risks to health are no longer negligible or risk to the environment is no longer reasonable, those risks can be reduced to levels that are negligible to human health by applying confinement practices. Under these circumstances, the Guidelines call for Level 2 confinement principles and safety protocols.

Dr. Witt indicated that he agreed with the consultants' summary. For him the two main issues are: 1) whether the modified fish are adequately confined, and 2) the risk of escape of transgenic catfish into the ecosystem. Dr. Witt felt that all reasonable confinement measures have been proposed, but that there is a real question as to whether the holding ponds for brood fish would be adequate if a flood occurred. He also said that likelihood is low that escaped fish would survive to sexual maturity.

Dr. Witt noted two inconsistencies in the proposal. First, the proposal indicates that the offspring would be killed before maturity, but later lists traits such as fecundity, sexual maturity, and rate of sexual maturity as points for evaluation. Second, with regard to the behavioral assessment, he questioned whether aggressiveness could be tied to a superior growth rate and expressed the opinion that at some point experiments to assess behavior will be needed.

Dr. Bruggeman spoke next. He noted that in his capacity as an expert for the National Audubon Society, he had written a letter to Dr. Jordan in the fall of 1991 asking that the catfish experiment be delayed until the carp experiment is completed.

Dr. Bruggeman felt that both the proposal and environmental assessment were inadequate, because there was an absence of sufficient data to support many of the proposal's assertions about the fitness of the catfish and their ability to cause

environmental impacts. He said that some of this data could be gathered from the carp experiments.

Dr. Bruggeman indicated that one way to manage risk in such experiments is to proceed in a step-by-step fashion from small field tests to large field tests. In addition to collecting data on commercially important attributes, data also should be collected on ecological attributes for application to future tests. Dr. Bruggeman said he was under the impression that one of the purposes of the carp field test was to serve as a model system and provide guidance for future tests in carp or other species.

Dr. Bruggeman also said that the discussion of variations in the data presented by the principal investigator (Dr. Dunham) make it clear that it is difficult to infer fitness or other attributes of catfish from experiments on carp.

Dr. Bruggeman pointed out that the catfish proposal came only five months after the carp experiment began, and that he had received tables of data only two weeks before the ABRAC meeting. The tables contained 15 pages of unexplained data. He said that USDA needs a better process for handling these applications, and data should not be submitted in such a raw fashion.

Finally, Dr. Bruggeman said, although the proposal discussed the benefits of transgenic fish to commercial agriculture, the ABRAC has been asked to confine its deliberations to the proposal's safety and not the risks associated with commercial use. Dr. Bruggeman said that if the benefits to commercial agriculture are being posited to justify the experiment, it is reasonable for the ABRAC to discuss the risks that may be involved with commercial aquaculture and the kinds of data that should be collected.

Dr. Kapuscinski spoke next. She said she was comfortable with almost all of the confinement measures and concurred with the consultants that the experiment should proceed. However, she was concerned about the scientific design of the experiment regarding determination of the effect of rtGH on behavior. Without proper protocols to measure behavior, Dr. Kapuscinski said she would be concerned that the next stage of research would lack unbiased data with respect to behavioral changes. She suggested that such data be collected early so that if behavioral changes develop, innovative ways to manage risk might be developed that would make commercial application possible.

Dr. Kapuscinski also said that while the overall quality of the environmental analysis was not very important for the purposes of this experiment, she was concerned that approval of this proposal would set an example of the quality expected of future environmental analyses. She said that it is important for USDA to use this proposal to set a good example for future

environmental assessments, especially with regard to larger-scale releases.

Dr. Kapuscinski also expressed concern over the safety of the brood ponds, and found it ironic that both the old and new ponds are called confined facilities. She wondered whether it would be difficult to move the adult fish to the new ponds.

Dr. Kapuscinski also suggested that screens or covers be put on the containers with the incubating eggs in the flow-through paddle-wheel troughs.

Dr. Kapuscinski felt that many statements that appeared to be factual were actually hypotheses that needed testing. In addition, some citations were inappropriate.

Dr. Kapuscinski said that the statement "no change in behavior was observed" should be removed from the proposal unless there are quantifiable data to back it up. She also felt that some of the sample sizes were too small and that better statistical analyses were needed.

Dr. Kline asked if any public attendee wished to make a statement. None of the visitors made any statements.

ABRAC Discussion of Catfish Proposal

Dr. Kline reminded the ABRAC that it needed to judge whether the biosafety of this research was acceptable, after which it could proceed to a discussion of other issues.

After some discussion in which the ABRAC appeared to agree that the confinement measures for the experiment were adequate, Dr. Andow moved that the ABRAC issue the following statement regarding the experiment:

> The ABRAC believes that the current proposal adequately ensures the safety to human health and the environment for Phase 3 of the proposed project because the confinement design and protocols are sufficient to prevent escape into the environment.

Dr. Kapuscinski seconded the motion, and the ABRAC approved it by a vote of 10 to 1.

Before the vote was taken, Dr. Bruggeman pointed out that the history of Auburn University's management of the fish facilities was not perfect, and that exotic species had been released into local waterways. Therefore, he recommended that the ABRAC wait until completion of the carp experiment so that there would be 12

to 15 months of data to demonstrate that no escapes could occur.

Dr. Pierce said he thought it was inappropriate to say that Auburn at one time might have been responsible for the release of such species. He said that the specific unit for the catfish experiment seemed to be adequately designed to protect against such release. He also pointed out that if the carp data really have no relevance to the catfish data, as Dr. Bruggeman had said earlier, there was no reason to wait for the carp experiment to be completed.

Dr. Bruggeman said that in terms of the escape from the facility, he thought the data were relevant, but that the ecological attributes and phenotype of the carp might not be relevant to the catfish experiment.

Dr. Dunham pointed out that if the exotic fish referred to by Dr. Bruggeman did originate from Auburn, there had been no attempt to keep them from escaping, and there was no lapse in administrative procedures.

Dr. Kline opened discussion on more general issues associated with the proposal, suggesting three areas for discussion: procedures; issues related to fate and effects analyses; and data needed to guide future work.

Dr. Harlander asked if fish experiments were occurring in other countries, and if so, whether such experiments were addressing behavioral effects. Dr. Kapuscinski replied that fish experiments recently have been conducted in Japan, Israel, China, and Scandinavia but that she did not know their content. She noted that there is a proposal under consideration by the Legislative Commission of Minnesota Resources to measure ecologically important traits in transgenic fish.

Dr. Bruggeman noted that USDA does not have the statutory authority to regulate genetically engineered fish, and that the application only has come to USDA because of the CSRS funding. He asked whether the public was notified of the proposal and suggested that there should be a clear procedure to notify the public and to solicit public comment.

Ms. Cordle responded that major items on the ABRAC agenda are published in the Federal Register Notice of the ABRAC meeting, and that the NEPA/CSRS regulations provide a framework and procedure within which to deal with these experiments. She warned that not every research proposal should be brought to the attention of the ABRAC. Dr. Bruggeman agreed that would be impractical.

Dr. Young said that USDA is very concerned about how to handle transgenic research, and that the Guidelines constituted a good

start toward addressing this issue. The question now is how to implement the Guidelines without singling out transgenic research – but still deal with risk. There is nothing inherently risky about the process of genetic modification, and organisms will need to be judged individually. What is needed is a procedure that minimizes the burden on the research community, but also has sufficient provisions for safety to protect the environment and human health. For now, all USDA agencies probably will ask the ABRAC to look at the transgenic fish proposals, but at some point this will no longer be practical.

Dr. Vidaver pointed out that it is necessary to deal with more than Federally-funded projects through a mechanism such as the Guidelines that everybody accepts.

Dr. Andow suggested that the IBC provide a statement that it would monitor the experiment. Drs. Sederoff, Vidaver, and Harlander agreed. Dr. Kapuscinski suggested that the IBC state in writing that it would take responsibility for monitoring the brood stock pond and containment, which she viewed as the weakest link in the proposed experiment. Dr. Kline indicated that the record should show a recommendation that a commitment letter be obtained from the IBC.

Dr. Andow said he was troubled that the ABRAC was asked to review only Phase 3 of the project. If the ABRAC had looked at other parts of the project it would have seen that the ponds for the brood fish were inadequate. Ms. Cordle said that USDA suggested that the ABRAC focus on Phase 3 because the NIH Guidelines had already addressed Phases 1 and 2. However, that suggestion did not imply that ABRAC could not comment on those phases.

Dr. Letourneau asked if the brood ponds were in danger of being flooded. Dr. Dunham said that the brood ponds also were contained and were located above the 100-year flood level. The new ponds had not been built because the old ones were deemed inadequate, but had been planned for a long time. However, concerns about the old ponds did influence the design of the new ponds.

Dr. Kapuscinski asked whether the ABRAC or OAB has a way to review IBC decisions. Dr. Young suggested that the ABRAC might recommend that USDA prepare procedures with regard to this type of situation. However, he noted that USDA's policy has been to accept NIH and IBC recommendations under the NIH Guidelines, and that difficulties could ensue if USDA began to contest those recommendations.

Dr. Andow noted that the Guidelines are oriented toward confinement. To argue that experiments are safe because the organism in question will not survive or the effects of the organism are negligible does not appear to be a major part of the

Guidelines. Environmental fate analysis must improve if environmental effects arguments are deemed necessary to ensure the safety of experiments. Currently such analyses are relatively poor and need strengthening for several reasons.

Dr. Letourneau asked if the ABRAC would feel as comfortable with the experiment if the confinement were slightly less strict but the arguments regarding environmental effect remained the same. She indicated that her approval of the experiment was based on satisfaction with the confinement procedures.

Dr. Sederoff said he believed that fears of the effects of experiment on the phenotype were exaggerated, and that no adverse effects to the environment would result.

Dr. Kapuscinski said that she would not be comfortable with the experiment if the confinement procedures were removed. She said that models might help provide more quantitative answers to the questions being dealt with by the ABRAC and the investigators.

Dr. Sederoff maintained that when compared with other transgenic animals, the existing variation for these fish fell within the ranges for existing fish. Dr. Kapuscinski asked if that were true for traits that Dr. Dunham had not dealt with, such as behavior.

Dr. Letourneau said that although the fish in the Auburn experiment probably would not affect the environment, the ABRAC needed to be concerned about the precedent being set by the ABRAC's approval of this proposal. She felt the proposal contained information gaps and general statements. Dr. Sederoff cautioned against holding proposals for transgenic experiments to a higher standard than proposals for non-transgenic experiments.

Dr. Young noted that Dr. Dunham had asked for funding to conduct risk assessment research with regard to his experiment. He suggested that the ABRAC letter on risk assessment stress this area of need.

Dr. Andow said that normal variations do not preclude the existence of problems. He stressed the need for clarity as to what the phenotype is, and said that the components of the phenotype might show extreme variation, even if the phenotype itself does not.

Dr. Parker said that if he were a fish farmer who was considering breeding transgenic fish but was facing containment costs, he would want to see significant results from transgenic breeding methods. He said that the current data do not show such results, and suggested that until they do, there was insufficient justification to spend on money on behavioral studies.

Dr. Kapuscinski pointed out that state fish regulatory agencies and some Federal agencies (e.g., U.S. Fish and Wildlife Service) are developing or implementing genetics policies because they are concerned about negative environmental impacts of stocking fish from different areas and with different gene pools.

Dr. Letourneau noted that traditional breeding methods also may pose problems, and that in achieving an equitable standard, all breeding methods should be evaluated according to a higher standard.

Dr. Andow suggested that to facilitate risk assessment it would be useful to think about the types of data that should be collected and at what stages of development of an organism such data should be collected.

Ms. Cordle suggested that because risk is linked to the organism and its characteristics, there is some merit in waiting until an organism appears to be promising, and no further changes in characteristics are planned. Dr. Kapuscinski said that, considering the variation in the catfish, it might be worthwhile to wait for another generation to develop because changes in characteristics after selection might occur. However, she cautioned against waiting too long to evaluate the risks of transgenic experiments. She recommended working to determine key traits that might have an impact on fitness, and finding ways to minimize risks.

Dr. Vidaver pointed out that the Guidelines deal with many of these questions. Dr. Kapuscinski said that information is needed to apply the Guidelines to the Auburn experiment.

Dr. Sederoff asked Dr. Dunham about his plans regarding other potential gene constructs. Dr. Dunham indicated that Auburn researchers were interested in possible new constructs, but that for now he was planning to evaluate this particular gene construct.

Wrap-Up and Recess

Dr. Kline suggested that the proposed letter to Acting Assistant Secretary Mussman on USDA's proposed Biotechnology Risk Research Assessment Program encourage research to answer the kinds of questions being posed by the ABRAC in its discussion of the transgenic catfish proposal. He asked Drs. Vidaver and Kapuscinski to draft a sentence stating such encouragement for incorporation into the letter.

Dr. Kline then recessed the meeting for the day at 4:30 p.m.

March 13, 1992

Dr. Kline reconvened the meeting at 9:08 a.m. He asked Drs. Price, Hill, and Vidaver to discuss the proposed conflict-of-interest statement to be added to the ABRAC operating procedures as item #12.

Conflict-of-Interest Statement

Dr. Pierce explained that the statement is designed to ensure that new members of the ABRAC are to avoid appearances of conflict of interest during their period of service.

Dr. Kapuscinski asked for a definition of "beneficial interest." Dr. Pierce explained that "beneficial interest" refers to a situation which might not lead to financial gain but could result in another benefit, such as a promotion.

Dr. Kapuscinski asked what would happen if the ABRAC were asked to discuss a trade secret which, if disclosed, would benefit her institution, but which she knew nothing about. Dr. Pierce said that a standard of reasonableness would prevail in such an instance.

Dr. Hill asked that ",or" be inserted in the third line of the statement between the words "for" and "the". In addition, the word "members" on the last line of the statement was changed to "member."

Dr. Vidaver moved that the ABRAC accept the conflict-of-interest statement as amended (See Appendix B). Dr. Letourneau seconded the motion, which passed unanimously.

Dr. Kline then introduced Dr. John Payne, the first speaker in the morning's presentation on APHIS biotechnology activities.

APHIS Biotechnology Activities

Dr. Payne explained that USDA, NIH, EPA, and FDA regulatory activities concerning biotechnology fall under the 1986 Coordinated Framework. In February 1991, the President's Council on Competitiveness elaborated on that policy and emphasized that regulations should be risk-based.

On February 27, 1992, the White House Office of Science and Technology Policy (OSTP) published in the Federal Register its statement on the "Exercise of Federal Oversight within Scope of Statutory Authority: Planned Introductions of Biotechnology Products into the Environment" (hereafter referred to as the OSTP scope document). This statement elucidates the previous two

statements, and helps the regulatory agencies to choose the least burdensome way to assure safety.

APHIS regulates biotechnology products under two statutes that have been in place for many years: the Federal Plant Pest Act (1957) and the Virus-Serum-Toxin Act (1913).

Dr. Payne then introduced Dr. Cyril Gay, who discussed APHIS's program to regulate veterinary biologics produced through biotechnology.

Animal biologics fall under three categories. Category One covers inactivated biologics which pose no risk or unique concern. Category Two covers products which contain live microorganisms which are modified by insertion of marker genes or deletion of genes that code for virulence or immunological markers. Category Three covers products which use live expression vectors to carry recombinant-DNA-derived sequences that code for immunizing antigens and/or other immune stimulants.

Since 1982, APHIS has approved 42 licenses for biotechnology products in Categories One and Two. Most of these licenses have been in Category One, but seven or eight Category Two products also have received licenses. No licenses have been approved for products in Category Three, but some products are being developed, and field trials have been approved for three such products.

Under APHIS procedures, every Category Two or Three product that bears no ecological or public health implications receives a standard review, while those with a potential for adverse ecological or public health implications receive a special review. Experts from outside the agency participate in special reviews.

Ms. Steinbock asked how the development of biotechnology affected the APHIS caseload. Dr. Gay responded that the effect has been tremendous.

Dr. Donna Molloy of APHIS then discussed APHIS procedures for the field testing of live recombinant DNA products. She said that Category Two or Three biologicals were evaluated at four progressively less restrictive containment levels on a case-by-case basis. She then outlined the specific information needed for such a case. As an example, she used the Wistar Institute's request to conduct a field trial of an oral rabies vaccine (a live vectored experimental product) in New Jersey.

Dr. Molloy said that Wistar had provided sufficient information to process the application. Although not approved, the draft environmental assessment for the product is under review. The draft assessment will be published for public comment.

Although Wistar is the only organization that has come to APHIS for approval of a live vaccine, a Belgian vaccine is being used in the EC. This vaccine has not been licensed, but the EC's review and licensing procedures differ from those of the United States.

Dr. Kline asked how APHIS incorporates public concern into its biotech regulatory work. Dr. Payne responded that the number of Freedom of Information Act (FOIA) requests filed regarding a particular issue is a good barometer, and that no government procedure can be based on science alone. Dr. Kline agreed, saying that the determination of acceptable risk is a public and political decision.

Dr. Kapuscinski said that public concern can serve as a balance to the scientific community, and help ensure that risk assessment is of the highest quality. Dr. Sederoff cautioned against allowing public pressure to compromise science.

Dr. Catherine Joyce then discussed APHIS procedures to review plants and microorganisms produced through biotechnology under the Plant Pest Act. She said that permits for genetically modified plants have been issued since 1987.

The permits cover known plant pests or organisms that have a plant pest component in their development. This component may be the gene of interest or any regulatory sequences derived from a plant pest or transformation method. Permits are needed before release, and in instances of interstate movement and importation. Courtesy permits can be issued for products which are not covered by regulations, but for which the applicant wants a review.

Dr. Joyce said that 208 permits have been issued, and 86 applications are pending. The issued permits cover approximately 340 sites.

Dr. Joyce then described the specific information needed before a permit can be issued, and the information an environmental assessment must include.

Dr. Vidaver asked if modified plants being field tested must always be destroyed, or if they can be fed to animals after a field trial is over. Dr. Joyce said that USDA is awaiting an FDA decision on the matter; that decision is expected shortly. She noted that some cotton products could be used for other purposes, but that use of biotech products for human and animal feed is an open question.

Dr. Letourneau asked if border rows still are being dealt with on a case-by-case basis. Dr. Joyce said that was true with regard to crops, but that some standards could be set. For example,

products involving corn require an isolation distance of 660 feet. For cotton, border row standards vary according to region.

Dr. Bruggeman asked what the process is for commercialization of biotechnology products. Dr. Payne responded that when the applicant determines that data is sufficient, he or she will ask APHIS to determine that the plant is no longer a "regulated article" because it exhibits no plant pest characteristics. APHIS has indicated that a public process that includes public hearings and comments will be used in conjunction with the processes of other agencies in addressing the commercialization issue.

Dr. Payne noted the deregulation of certain areas for movement permits, and mentioned plant pest sequences containing *E. coli* and *Arabidopsis*.

Dr. Payne asked the ABRAC if there is sufficient experience to identify entire categories of plants or microorganisms that no longer need to be permitted for movement (e.g., from one contained facility to another) and where a notification to the public rather than a permit would be appropriate. Drs. Andow and Kapuscinski said they could not answer that question until they knew more about what information APHIS has. Dr. Bruggeman said that notification might be a good idea but that a specific proposal would be needed.

Dr. Payne said that he was not looking for an ABRAC seal of approval. He expressed interest in exploring the possibility of notification as distinguished from regulatory review of certain categories of organisms based on ABRAC's experience with reviewing the safety of parental organisms, genetic changes, modified organisms, specific environments, and confinement measures. He posed the question rhetorically as "Do you agree in principle with that kind of approach, not any specific notification scheme?"

Dr. Young inquired, if ABRAC took the initiative of looking at a specific area where there has been extensive field testing and assembled data and assessed it, whether APHIS would accept that as a basis for a regulatory exclusion. Dr. Payne replied that he would prefer to see ABRAC as a scientific committee that could judge on the basis of science without getting into a procedural position on these issues. He referred to regulatory constraints that would make it difficult for APHIS to discuss specific regulatory proposals in a public meeting such as ABRAC.

Ms. Cordle referred to a legal interpretation that, up until the time of publication of an agency proposal, the agency is free to consult with anyone it wishes in developing thoughts on what to propose. Dr. Payne replied that that is what he is doing before the ABRAC. He reiterated the question of ABRAC views on

proceeding in the direction of notification as an alternative to regulatory review.

Dr. Vidaver said that a notification under contained lab conditions was a good idea, and noted that agriculture is subject to stricter permitting conditions than the medical community is. She suggested that a temporary notification scheme in one region of the country could be attempted to see if there is any difference.

Dr. Kline asked Dr. Payne if he would be willing to sit down with the ABRAC at a future meeting and work out how the ABRAC might work with APHIS. Dr. Payne replied that, since the ABRAC advises the Assistant Secretary for Science and Education, that would be appropriate for scientific issues but not for regulatory procedural issues.

Dr. Young said Dr. Payne's interpretation was incorrect. Dr. Young said ABRAC's responsibility is to provide advice to the Secretary who views the ABRAC as an advisory mechanism for the Department of Agriculture, not just for Science and Education. It is an administrative expedient, he said, that ABRAC recommendations go first to the Assistant Secretary for Science and Education because the name of the Committee contains the word "Research." He also referred to a General Counsel opinion that reporting through Science and Education in no way limited ABRAC advice to Science and Education.

Dr. Payne replied that because of that opinion, he was here before the ABRAC seeking scientific advice on a principle, not a proposal. He said there are ways of working within the procedural constraints on APHIS and that ABRAC should expect a closer relationship in the future.

Ms. Cordle asked if the Guidelines' lowest level of safety concern for a modified organism would lend itself to a notification scheme. Dr. Payne replied it would be possible if, as the current [OSTP] policy statement indicates, there are appropriate mechanisms in place for local review. He cautioned against duplicate reviews, stressed the need for interagency coordination, and added that APHIS cannot delegate authority to the IBC's under the Plant Pest Act.

Dr. Kline thanked Dr. Payne, and after a short lunch break, introduced Dr. Robert Frederick of EPA's Risk Assessment Branch.

Dr. Robert Frederick: EPA Risk Assessment Program

Dr. Frederick said that EPA's risk assessment program started eight years ago and at first dealt strictly with genetically

modified microorganisms. Until the passage of the 1990 Farm Bill, it was the only biotechnology risk assessment program in the Federal government. The program has an annual budget of $6.9 million with which it enters into cooperative agreements with universities.

EPA's research is moving from smaller- to larger-scale issues, such as the effects of commercial release, and the agency is developing a long-term strategy.

About 155 pre-proposals for research have been submitted to EPA, from which 25 were selected for request for full proposals. Several additional proposals were reviewed with Environment Canada. Three to five academic experts review the pre-proposals and proposals for scientific merit.

Dr. Kline thanked Dr. Frederick, and directed the ABRAC to the draft letter to Acting Assistant Secretary Mussman on USDA's risk assessment efforts.

Letter to Dr. Mussman

Dr. Andow moved that the ABRAC send a letter to Dr. Mussman, with the changes outlined below, which reviews USDA's proposed Biotechnology Risk Assessment Research Program. Dr. Kapuscinski seconded the motion. The motion passed unanimously.

The changes in the draft (Appendix C) to which the ABRAC agreed are:

- In the first bulleted paragraph, substitution of the word "quantification" for "qualification," and substitution of the word "affect" for "effect;"
- In the paragraph after the bulleted paragraph, changing the first line to read: "Incorporating risk assessment research into product research and development work ... "; and
- In the third line of the last paragraph on the first page, deleting the words "the new", and substituting the term "e.g." for "i.e."

Dr. Kline then asked Ms. Cordle to discuss the OSTP scope document.

OSTP Scope Document

Ms. Cordle said that the OSTP scope document was the result of four years' work, and that it had been reviewed and adopted by the Council on Competitiveness chaired by the Vice President.

The document gives no new authorities, but addresses agency discretion regarding the introduction of biotechnology products into the environment.

Ms. Cordle noted that the OSTP document is designed to apply to all stages of an introduction (i.e., research through development and commercialization), and to all products, not just to new products. The exclusion categories previously proposed were dropped.

The key points of the document are:

- Agencies should act only if the risk posed by introduction of biotechnology products into the environment is unreasonable.

- Agencies should aim to achieve the greatest risk reduction at the least possible cost.

- Choices from among options for oversight should be made according to risk.

Ms. Cordle said that one way to judge risk is to compare the risk with that of previously used or introduced comparable species. The introduction should be subject to no more oversight than earlier comparable introductions in a comparable environment. The idea is to assess the products, not the process.

Ms. Cordle noted that the OSTP document cites the USDA Guidelines as an example of the hierarchical approach to oversight that OSTP recommends.

Dr. Kline asked what the status of the USDA Guidelines was. Ms. Cordle said the final example for the Appendix had been submitted only a week ago, and that she was working on the preamble. She said that she was very encouraged to see that the OSTP scope document supports many of the concepts in the Guidelines.

Dr. Young said that Dr. Mussman was anxious to see the Guidelines appear in the Federal Register, and that the ABRAC's recommendations for the Guidelines would be published separately. He warned that the version of the Guidelines which appears in the Federal Register may differ from what ABRAC recommends.

Dr. Kapuscinski said that the carp example in the Guidelines contains a major scientific error which needs to be corrected. Dr. Young said the error would be corrected.

Dr. Kline then asked Dr. Young to discuss the proposed evaluation study for developing standards for outdoor ponds for transgenic fish, and other possible ABRAC initiatives.

Future ABRAC Initiatives

Dr. Young said that standards for ponds might have forestalled the previous day's protracted debate on the Auburn University transgenic catfish proposal. He recommended that an ABRAC working group be established to develop such standards.

Dr. Young also suggested that the ABRAC consider forming work groups to consider risk assessment (Dr. Andow had chaired a work group in this area, with Dr. Kline and Dr. Lee Bulla as members), as well as priority-setting groups in specific areas such as aquaculture, food safety, and socioeconomic impacts of biotechnology.

Dr. Kapuscinski said she already had begun to work on a proposal for standardizing construction of outdoor ponds and other fish holding facilities, and had talked with Sea Grant and Dr. Young about it. She wanted to see a small group develop a draft document, then invite up to 25 people to a workshop to discuss the draft.

Dr. Young said that the final version of the standards could be published in the Federal Register, and noted that Secretary Madigan chairs the Federal interagency aquaculture committee. Dr. Kapuscinski said that the American Fisheries Society and the fisheries industry would support such an effort.

With regard to the priority-setting groups, interest was indicated as follows:

Dr. Andow said he would continue to chair a risk assessment working group; Dr. Witt indicated an interest in the outdoor ponds group; Dr. Sederoff, socioeconomic group; Dr. Bruggeman, risk assessment; Dr. Harlander, food safety (including value-added products); Dr. Vidaver, socioeconomic or risk assessment; Dr. Hill, socioeconomic or food safety group; Dr. Letourneau, socioeconomic group; and Dr. Pierce, food safety.

Dr. Letourneau asked to speak about the previous day's discussion of the transgenic catfish proposal.

Further Discussion of Transgenic Catfish Proposal

Dr. Letourneau said that she felt the tone of the proposal led the ABRAC to strongly criticize it. The proposal extended the limited data available to make the best possible predictions of environmental risks associated with the experiment. Another approach might have been to point out clearly what kinds of data and information were missing, and suggest experiments to be performed to fill those gaps.

Dr. Sederoff said that the principal investigator didn't realize what was important to the ABRAC. Investigators who make subsequent presentations to the ABRAC should be given a clearer idea of what the ABRAC wants to hear about, and should be given the Guidelines to help them focus their presentations.

Dr. Young pointed out that the proposal was written not for the ABRAC but for CSRS, and that Dr. Jordan made the decision to bring the proposal to the ABRAC. Ms. Cordle noted that the Auburn investigators did not have the Guidelines to help them because the Guidelines had not yet been adopted.

Dr. Kline pointed out that the science in the proposal had not been very good, and Dr. Kapuscinski added that good science is important to risk-based management. Dr. Bruggeman agreed, saying that adhering to the Guidelines would not have solved the problems with the Auburn proposal.

Dr. Sederoff suggested that the ABRAC develop a one-page description of the information proposals presented to the ABRAC should contain, and that such descriptions refer to NEPA and the Guidelines. Dr. Kline suggested that the matter be taken up at another date.

Future ABRAC Meetings

Dr. Young reminded the ABRAC of proposed future meeting dates: June 10-12; September 23-24; and December 9-11. The ABRAC agreed with Dr. Young's suggestion to hold the September meeting in Denver.

Dr. Kline adjourned the meeting at 2:55 p.m.

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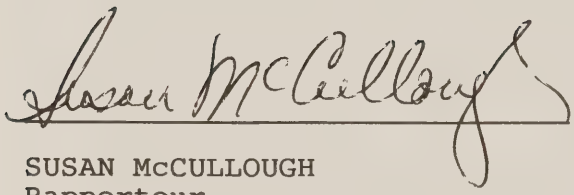
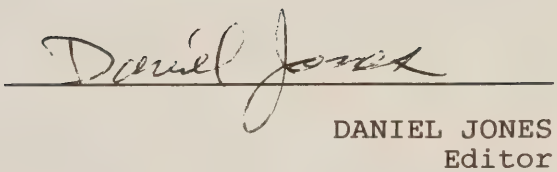
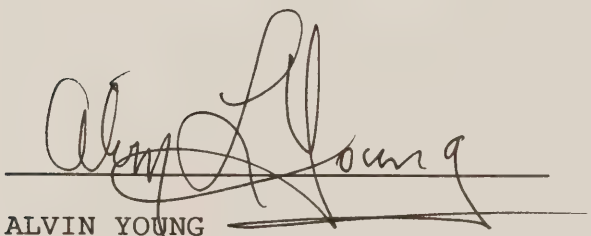
Approved:



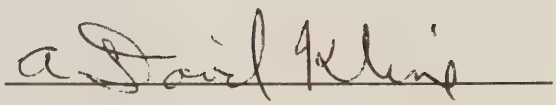
SUSAN McCULLOUGH
Rapporteur



DANIEL JONES
Editor



ALVIN YOUNG
Executive Secretary



A. DAVID KLINE
Chair

APPENDIX A

LIST OF VISITORS
UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL BIOTECHNOLOGY RESEARCH ADVISORY COMMITTEE
Meeting of March 11-13, 1992

John Irwin, University of Maryland
Chris Plein, University of Missouri
Lisa Zannoni, Office of the Secretary, USDA
Jim Rasek, Food Safety and Inspection Service, USDA
Cassandra Klotz, Economic Research Service, USDA
Kelly Day, Economic Research Service, USDA
Pedro Barbossa, Ecological Society of America
Ken Reid, Food Chemical News
Bharat Patel, Food Safety and Inspection Service, USDA
David Berkowitz, U.S. Food and Drug Administration
Sarah Crim, Bureau of National Affairs
Debbie Olson, Stanford Research Institute
Kathy Hudson, Department of Health and Human Services
Bob Warmbroldt, National Agricultural Library, USDA
Don Downer, Mississippi State University
Margaret Egan, ASCI Corporation
Clarence Hanes, Agricultural Marketing Service
Pat Basu, Food Safety and Inspection Service, USDA
Urban Oto, Food Safety and Inspection Service, USDA
Jeffrey Fox, ASM News
Margaret Mellon, National Wildlife Federation
Natasha DeWees, Huntsville News
Elliott Entis, A/F Protein, Inc.
Peter Dearborn, University of Maryland
Robert G. Zimbelman, American Society of Animal Science
Harry Mussman, Office of the Secretary, USDA
Edward Wilson, Cooperative State Research Service, USDA
Arthur Kelman, Cooperative State Research Service, USDA
Ann Lichens-Park, Cooperative State Research Service, USDA
Jay Blowers, Cooperative State Research Service, USDA
Stanley Krugman, Forest Service, USDA
John Reilly, Economic Research Service, USDA
Marvin Norcross, Food Safety and Inspection Service, USDA
Rex Dunham, Auburn University
Charles Brown, Animal and Plant Health Inspection Service, USDA
Meryl Broussard, Cooperative State Research Service, USDA
Nick Parker, Texas Tech University
William Reeves, Alabama Department of Conservation and Natural Resources
John Payne, Animal and Plant Health Inspection Service, USDA
Cyril Gay, Animal and Plant Health Inspection Service, USDA
Donna Molloy, Animal and Plant Health Inspection Service, USDA
Catherine Joyce, Animal and Plant Health Inspection Service, USDA
Robert Frederick, U.S. Environmental Protection Agency

ABRAC intentionally contains within its membership people of diverse opinions and affiliations, which requires that its members be cognizant of the potential for, or the appearance of conflicts of interest. Accordingly, although opinions can and should be presented in order to ensure that diversity, ABRAC members should abstain from voting on any issue in which the members may have a financial or other beneficial interest, whether directly or indirectly.

Similarly, members should refrain from receiving any confidential information and/or trade secrets relating to a matter in which the members or the member's affiliation competes.

Approved by voice vote
3/13/92

*U.S. G.P.O.:1992-341-418:60052